IN THE CLAIMS:

Please *cancel* claims 1-19, and *add* the following new claims:

20. A process for changing the expression of a nucleic acid sequence which is present endogenously in a eukaryotic cell, the method comprising

(a) transfecting the cell with a vector comprising

(i) at least one sequence selected from the group consisting of a heterologous expression control sequence and an amplification gene,

(ii) a positive selection marker gene,

(iii) at least two target sequences for a site-specific recombinase flanking the sequences (i) and (ii), and

(iv) DNA sequences which flank the sequences (i), (ii) and (iii) and are homologous to a nucleic acid section in the genome of the cell in order to allow a homologous recombination,

(b) culturing the transfected cell under conditions under which a homologous recombination of the vector takes place,

(c) isolating the cell obtained according to step (b), and

(d) expressing the heterologous expression control sequence under conditions under which the expression of the nucleic acid sequence which is present endogenously in the cell is changed.

21. The process as claimed in claim 20, wherein the site-specific recombinase target sequences are loxP sequences.

22. The process as claimed in claim 20, wherein the vector further comprises a negative selection marker gene which is located outside the homologous DNA sequences (iv).

23. The process as claimed in claim 20, further comprising, after step (d), cutting the sequences (i) and (ii) flanked by the site-specific recombinase target sequences out of the genome of the cell by transient activation of a site-specific recombinase that recognizes the target sequences.

24. A vector suitable for homologous recombination, comprising

(i) at least one sequence selected from the group consisting of an expression control sequence and an amplification gene,

(ii) a positive selection marker gene,

(iii) at least two target sequences for a site-specific recombinase flanking the sequences (i) and (ii), and

(iv) DNA sequences which flank the sequences (i), (ii) and (iii) and are homologous to a nucleic acid section in the genome of a cell in order to allow a

homologous recombination, and

(v) optionally a negative selection marker gene.

25. A vector, comprising

(i) at least one sequence selected from the group consisting of a heterologous expression control sequence and an amplification gene,

(ii) a positive selection marker gene,

(iii) at least two recombinase target sequences flanking the sequences (i) and (ii), and

(iv) optionally a negative selection marker gene.

26. A eukaryotic cell, comprising

(a) at least one chromosomally-located sequence selected from the group consisting of a heterologous expression control sequence and an exogenous amplification gene in operative linkage with a nucleic acid sequence which is present endogenously in the cell, and

(b) recombinase target sequences flanking the sequence (a).

27. The eukaryotic cell of claim 26, wherein the cell is a human cell.

28. A process for changing the expression of a nucleic acid sequence which is present endogenously in a eukaryotic cell, the method comprising

(a) transfecting the cell with a vector comprising

(i) at least one nucleic acid sequence which binds an activator protein,

(ii) a positive selection marker gene, and

(iii) DNA sequences which flank the sequences (i) and (ii) and are homologous to a nucleic acid section in the genome of the cell in order to allow a homologous recombination,

(b) culturing the transfected cell under conditions under which a homologous recombination of the vector takes place,

(c) isolating the cell obtained according to step (b), and

(d) expressing the sequence (i) under conditions under which the expression of the nucleic acid sequence which is present endogenously in the cell is changed.

29. The process as claimed in claim 28, wherein the sequence (i) is a hypoxia-inducible factor-binding nucleic acid sequence.

30. A eukaryotic cell obtainable by the process as claimed in claim 28.

31. The eukaryotic cell of claim 30, wherein the cell is a human cell.

32. A vector suitable for homologous recombination, comprising

(i) at least one nucleic acid sequence which binds an activator protein,

(ii) a positive selection marker gene, and

(iii) DNA sequences which flank the sequences (i) and (ii) and are homologous to a nucleic acid section in the genome of a cell in order to allow a homologous recombination.

33. A eukaryotic cell, comprising at least one chromosomally-located exogenous nucleic acid sequence which binds an activator protein/activator protein complex which is operatively linked with a gene which is present endogenously in the cell.

34. The eukaryotic cell of claim 33, wherein the cell is a human cell.

35. A process for testing the influence of non-coding nucleic acid sequences from the region of a target gene present endogenously in a eukaryotic cell on its expression, the process comprising

(a) transfecting the cell with a vector comprising

(i) a heterologous expression control sequence which is active or can be activated in the cell and is operatively linked with a reporter gene, and

(ii) non-coding nucleic acid sequences on the 5'-side and/or the 3'-side from the region of the target gene,

(b) culturing the cell under conditions under which the expression control sequence is active, and

(c) measuring the expression of the reporter gene.

36. A process for obtaining a DHFR-negative eukaryotic cell, the process comprising

(a) transfecting the cell with a first vector comprising

(i) at least one target sequence for a site-specific recombinase;

(ii) DNA sequences which flank sequence (i) and are homologous to a DHFR nucleic acid sequence which is present endogenously in the cell in order to allow a homologous recombination,

(iii) optionally a first positive selection marker gene, and

(iv) optionally a negative selection marker gene,

(b) culturing the transfected cell under conditions under which a homologous recombination of the vector takes place, and

(c) isolating the cell obtained according to step (b) to obtain a DHFR-negative eukaryotic cell.

37. A process for obtaining a eukaryotic cell containing a nucleic acid sequence to be amplified and a heterologous DHFR gene, the process comprising

(a) obtaining a DHFR-negative eukaryotic cell by the process as claimed in claim 36,

(b) transfecting the cell of step (a) with a second vector comprising

(i) a nucleic acid sequence coding for a DHFR,

(ii) a nucleic acid sequence to be amplified which codes for a protein in an expressible form,

(iii) optionally a second positive selection marker gene, and

(iv) at least two recombinase target sequences flanking the sequences (i), (ii) and (iii), if present,

(c) culturing the transfected cell under conditions under which the sequences (i), (ii) and (iii), if present, are integrated into the recombinase target sequence that is already present in the genome of the cell, and

(d) isolating the cell obtained according to step (c) to obtain a eukaryotic cell containing a nucleic acid sequence to be amplified and a heterologous DHFR gene.

38. The process of claim 37, wherein the second positive selection marker gene differs from the first positive selection marker gene.

39. A vector, comprising

(i) a nucleic acid sequence coding for a DHFR,

(ii) a nucleic acid sequence to be amplified which codes for a protein in an expressible form,

(iii) optionally a positive selection marker gene, and

(iv) at least two recombinase target sequences flanking the sequences (i), (ii) and (iii), if present.

40. A vector suitable for homologous recombination, comprising

(i) optionally a positive selection marker gene,

(ii) at least one recombinase target sequence which flanks the sequence (i), if present,

(iii) DNA sequences which flank the sequences (i), if present, and (ii) and which are homologous to a DHFR nucleic acid sequence which is present endogenously in a cell in order to allow a homologous recombination, and

(iv) optionally a negative selection marker gene which is outside the homologous DNA sequences (iii).

41. A eukaryotic cell, comprising

(a) at least one inactivated endogenous nucleic acid sequence coding for a DHFR, and

(b) at least one recombinase target sequence which is integrated into the genome in the region of the sequence (a).

42. The eukaryotic cell of claim 41, wherein the cell is a human cell.

43. A eukaryotic cell, comprising a heterologous nucleic acid sequence in the region of an endogenous DHFR gene locus, the heterologous sequence comprising

(i) a nucleic acid sequence coding for a DHFR,

(ii) a nucleic acid sequence coding for a desired protein, and

(iii) at least one recombinase target sequence.

REMARKS

Claims 1-19 are currently pending. In this Response, applicants cancel claims 1-19, and add new claims 20-43.

The Examiner notes that a Sequence Listing has not been filed, and that a sequence appears at page 36 of the specification. Applicants attach hereto a Sequence Listing, and have amended the specification accordingly.

Claims 1, 7, 8, 11, 13-16 and 19 are rejected under 35 USC §112, second paragraph, as being indefinite.